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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Ijeoma Uchegbu

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EXAMINER

GREENE, IVAN A

ART UNIT

PAPER NUMBER

1619

MAIL DATE

DELIVERY MODE

08/04/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/528,602	Applicant(s) UCHEGBU ET AL.	
	Examiner IVAN GREENE	Art Unit 1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,32,33,44 and 46-48 is/are pending in the application.
- 4a) Of the above claim(s) 1-3,32 and 33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 44 and 46-48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 21 March 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/20/2005; 08/22/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the claims

Claims 1-3, 32, 33, 44, and 46-48 are currently pending. Claims 4-31, 34-43 and 49-57 have been canceled. Claims 1-3, 32 and 33 have been withdrawn base upon restriction, discussed below. Claims 44 and 46-48 are under examination.

Restriction

Applicant's election with traverse of group three in the reply filed on 02/27/2009 is acknowledged. The traversal is on the ground(s) that the common monomeric subunits that make up the claimed polyethylene polymer are the special technical feature. This is not found persuasive because the claimed polymer is a random or block copolymer and the defining characteristics of a block copolymer are typically very different from those of a random polymer. Furthermore, applicant has not provided evidence that the claimed random and block copolymers have similar characteristics.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-3, 32 and 33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 02/27/2009.

The requirement for species election has been removed because applicant's elected a species does not include each of the subunits α , β , and γ as (as defined in claim 1). The polymer is being examined for any species which reads on the genus.

Information Disclosure Statement

The information disclosure statement(s) submitted on 12/20/2005 and 08/22/2006 were filed before the mailing date of the first office action on the merits. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the Examiner.

Priority

The U.S. effective filing date has been determined to be 09/22/2003, the filing date of the document PCT/GB03/04036. The foreign priority date has been determined to be 09/20/2002, the filing date of document GB-0221942.6.

Objections

Claims 44 and 46-48 are objected as being dependent on withdrawn claim 1. The claim(s) should be rewritten in independent form, as appropriate.

Rejections

Claim Rejections - 35 U.S.C. 112

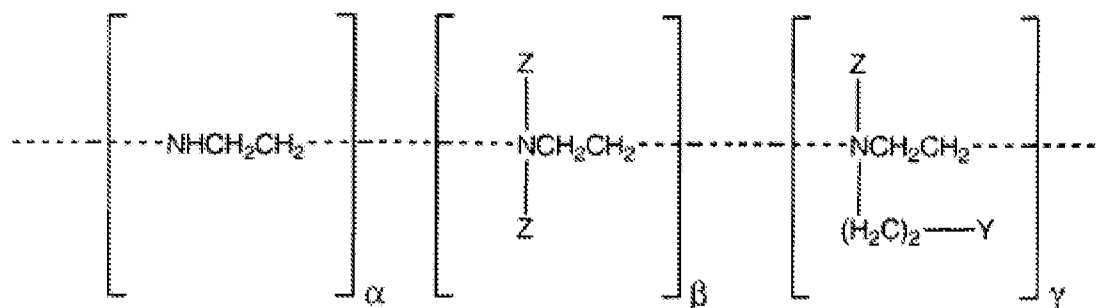
The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 44 and 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

2. Claim 44 is rejected as being indefinite because it is unclear what exactly the metes and bounds of the recited polymer genus are. The claim recite a polymer according to claim 1 wherein the formula is:

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wherein α is between 0 to 90%;

β is between 0 to 100%;

γ is between 0 to 50%;

wherein $\alpha + \beta + \gamma = 100\%$; and

The polymer formula is indefinite for the following three reasons: first the quaternary nitrogen atoms should include a positive charge; second it is unclear what exactly the proportion of each subunit in a species of the polymer genus should be; third, the claim recites --the Z groups are hydrophobic and are independently hydrogen--. A hydrogen is generally not considered hydrophobic in nature.

3. Claim 44 is further rejected as being indefinite because the claim recites “a polyethylenimine polymer,” and a “pharmaceutically acceptable carrier.” The polyethylenimine polymer is indicated as a drug carrier (instant specification, [0030]). It is unclear whether the claim refers to the polyethylenimine polymer as the pharmaceutically acceptable carrier or requires the further addition of another pharmaceutically acceptable carrier.

4. Claim 44 is further rejected as being indefinite because the claim recites “Y may represent a hydrophilic substituent.” The phrase “may represent” renders the claim indefinite because it is unclear whether the limitation following the phrase is required.

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5. Claim 47 is rejected as being indefinite because the claim recites "such as" which renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention (MPEP 2173.05(d)).

6. Claim 48 is rejected as being indefinite because the claim recites "such as" which renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention (MPEP 2173.05(d)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

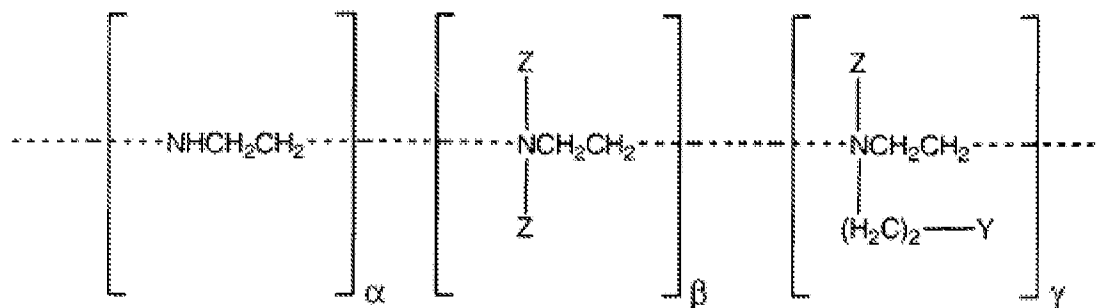
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under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 44 and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over WANG (Biomacromolecules, 2002, Vol. 3, pp. 1197-1207) in view of KURONO (US 4,528,184) and YOKOYAMA (US 2001/0014354).

Applicants Claims

Applicant claims a composition comprising a polyethylenimine (PEI) polymer according the following formula:



wherein α is between 0 to 90%;

β is between 0 to 100%;

γ is between 0 to 50%;

wherein $\alpha + \beta + \gamma = 100\%$; and

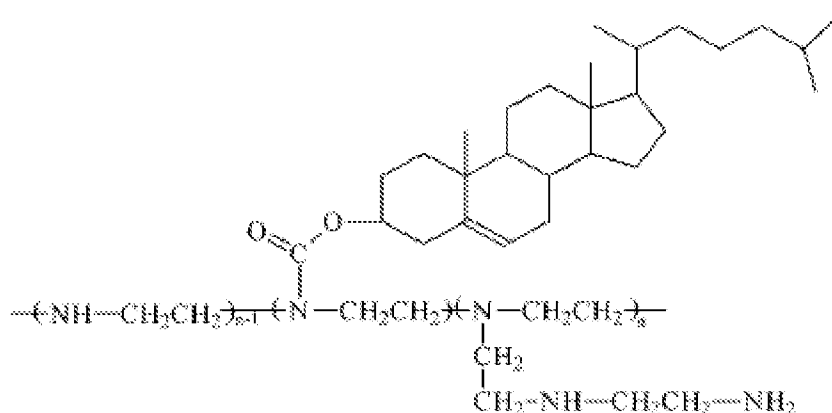
where Z groups are hydrophobic and are independently hydrogen or any linear or branched, substituted or unsubstituted, or cyclo form of any hydrophobic substituent; and Y may represent a hydrophilic substituent; and wherein the composition is a

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pharmaceutical drug carrier for poorly soluble drugs such as the anti-cancer drug paclitaxel.

**Determination of the scope
and content of the prior art (MPEP 2141.01)**

WANG teaches branched PEI-cholesterol water-soluble lipopolymers for gene delivery (title). WANG further teaches the PEI-cholesterol lipopolymer is amphiphilic in nature because PEI is hydrophilic and water-soluble, while cholesterol is hydrophobic (p. 1200, col. 2, lines 24-27). WANG teaches the following PEI-cholesterol polymer (p. 1200, Figure 1):



WANG further teaches PEI-cholesterol forms micells which can encapsulate hydrophobic molecules when concentration in water is greater than the critical micellar concentration (p. 1202, col. 1, lines 1-7). WANG further teaches that it is known that PEI contains all three kinds, primary, secondary and tertiary amines whose pK_a value is not easily assigned because the effects of local groups lead to different ionization constants for every amino group (p. 1201, col. 2, lines 7-11). WANG further teaches PEI molecules exist either as a linear or a branched form, and have very high charge-

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potential with every third atom as an amino nitrogen that can be protonated (p. 1205, col. 2, lines 20-23).

**Ascertainment of the difference between
the prior art and the claims (MPEP 2141.02)**

The difference between the rejected claims and the teachings of WANG is that WANG does not expressly teach the poorly water soluble drug species paclitaxel; or the quaternary nitrogen atoms of the PEI-type polymers. This deficiency in paclitaxel is cured by the teachings of YOKOYAMA. And the deficiency in the quaternary nitrogen atoms of the PEI-type polymers is cured by the teachings of KURONO.

YOKOYAMA teaches the present invention relates to a production process for a polymeric micelle charged therein with a [poorly water] soluble drug ([0001]). YOKOYAMA further teaches it is known to use a block copolymer having a hydrophilic segment and a hydrophobic segment for a drug carrier and how to charge a micelle formed by the copolymer with a [poorly water soluble] drug ([0002]). YOKOYAMA further teaches the poorly water soluble drugs testosterone and paclitaxel ([0017]).

KURONO teaches the novel polymer-metal complex containing quaternary nitrogen atoms and process for their production and use as a pharmaceutical product (1:5-10). KURONO further teaches among the methods for quaternizing the nitrogen atoms in the polymer the most popular one is to treat with alkylating agent e.g. methyl iodide, and repeating the alkylation the, the proportion of quaternary nitrogen atoms increases gradually (3:18-24).

Finding of *prima facie* obviousness

Rationale and Motivation (MPEP 2142-2143)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine YOKOYAMA and KURONO with WANG and produce the instantly claimed invention because the poorly soluble drugs taught by YOKOYAMA would have been suitable for the gene delivery micellar composition of WANG and the increased charge of the nitrogen atoms in the PEI-type polymers of WANG would have increased the interaction with the poorly water soluble drug providing an increased loading of the drug into the micelle. Furthermore, the charges of the quaternary nitrogen atoms would have allowed the formation, potentially more stable and/or efficacious salts, of salts of poorly soluble drugs. One of ordinary skill in the art would have been motivated to produce an amphiphilic quaternary PEI-type polymer suitable for poorly water soluble drug delivery because the polymer would have had an increased efficacious action leading to increased sales of the drug product.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

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In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

Conclusion

Claims 44 and 46-48 have been examined on the merits. Claims 44 and 46-48 are rejected under 35 U.S.C. 112, second paragraph; and claims 44 and 46-48 are rejected under 35 U.S.C. 103(a). No claims allowed at this time.

The examiner requests that, upon reviewing the instant office action, the applicant contact the examiner to arrange an interview to discuss the claims and how best to overcome the rejections, as discussed above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to IVAN GREENE whose telephone number is (571)270-5868. The examiner can normally be reached on Monday through Thursday 7AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

IVAN GREENE

Examiner, Art Unit 1619

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616